REMARKS

Applicants have amended claims 1, 4, 7 and 13 to recite the administration dose and concentration of the essential amino acids necessary for suppressing proliferation of prion proteins. Support for these amendments is found e.g., on page 6, lines 21-27.

Claims 7 and 9 stand rejected under 35 U.S.C. 102(b) for purportedly being anticipated by Richardson (WO96/21437). In view of the amendments to the claims and the following remarks Applicants request that the Examiner reconsider and withdraw the rejection.

Claim 7 have been amended to recite:

> A suppressive agent containing an essential amino acid having a branched side chain as an active ingredient for suppressing proliferation of abnormal prion proteins wherein the essential amino acid having a branched side chain is selected from the group consisting of leucine, isoleucine, valine, and mixtures thereof and wherein the essential amino acid in the suppressive agent is 20 to 40 mg/mL of the suppressive agent.

Richardson fails to teach a suppressive agent containing the specific essential amino acids recited in the claims at the specific concentration, 20-40mg/mL, recited in the claims and therefore does not anticipate independent claim 7 or dependent claim 9, which depends on claim 7.

In view of the foregoing remarks and amendment to the claims, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 102(b) for being anticipated by Richardson.

Claims 1, 3, 4, 6, 13 and 15-19 stand rejected under 35 U.S.C. 103(a) for purportedly being obvious over Richardson (WO 96/21437) as applied to claims 7 and 9 in the 102(b) rejection above in view of Gordon (WO 00/64420). Applicants

disagree and in view of the amendments to the claims and the following remarks request that the Examiner reconsider and withdraw the rejection.

Applicants have amended claims 1, 4, and 13 to recite the administration dose necessary for suppressing proliferation of prion proteins is 5-15g/kg, and concentration of the essential amino acids necessary for suppressing proliferation of prion proteins is 20-40mg/mL. Support for these amendments is found e.g., on page 6, lines 21-27.

Prior to Applicants' invention, the effect of the particular branched amino acids on prion proliferation was unknown. Neither Richardson nor Gordon teach or suggest that administration of essential amino acids has any effect on the proliferation of prion proteins. Richardson discloses that 50-1500mg/kg (0.05-1.5g/kg) is sufficient for alleviating TD symptoms. However, this is not a teaching or suggestion that such an amount would inherently affect prion proliferation.

> To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' "
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> *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)

All of Richardson's research is based on subjects not infected with prion proteins and is directed to adjusting the levels of plasma phenylalanine. Furthermore, the concentrations of amino acids in Richardson's methods are outside the ranges recited in Applicants' claims. Thus it can not be concluded that the method taught by Richardson inherently suppresses prion proliferation.

Furthermore, Richardson at best only provides a general approach that may have seemed a promising field of experimentation in the treatment of abnormal movement disorders associated with an imbalance in phenylalanine, but such is not sufficient to establish obviousness.

> The second class of O'Farrell's impermissible "obvious to try" situations occurs where what was "obvious to try" was to explore . . . or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. 853 F.2d at 903.
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> Cited in *In re Kubin* (Fed Cir 2009)

One of skill in the art could not reasonably predict from Richardson's disclosure that combinations of aromatic or branch chain amino acids, i.e., leucine, isoleucine and valine, in an amount sufficient to alleviate abnormal movement would have any effect on the other diseases disclosed in Richardson. Richardson acknowledges the "complexities of treatment in this field..." page 42, line 25, and in fact Richardson spent ***15 years*** studying one type of condition, neuroleptic-induced abnormal movement disorders, to generate a unitary paradigm (page 4 lines 12-37) and still after 15 years of study could only speculate about the effects of aromatic and branch chain amino acids on plasma phenylalanine and a suspected correlation with TD (page 13, line 5 to page 15, line 19). Richardson hypothesized that the levels of phenylalanine accumulated in the plasma and tissues of psychiatric patients play a role in whether such a patient will develop abnormal movement disorders, such as tardive dyskinesia, secondary to treatment with neuroleptic drugs (page 15, lines 20-26). Richardson speculates that patients with TD may be experiencing small but regular relatively higher elevations in plasma phenylalanine (page 15, lines 27-30): Yet Richardson or Gordon fail to provide any evidence that subjects with CJD or any other recited prion conditions have elevated levels of plasma

phenylalanine and therefore would benefit from the administration of aromatic or branched chain amino acids. Thus, Richardson simply provides at best only a general approach that seemed to be a promising field of experimentation and invites one of skill in the art to conduct further experiments. Such is not enough to establish obviousness.

The foregoing remarks demonstrate Richardson does not teach a method that inherently suppresses prion proliferation and that the combination of Richardson and Gordon also fails to suggest to one of skill in the art that prion proliferation could be suppressed by systemically, orally, intracerebrally or intraspinally administering to a patient in need thereof leucine, isoleucine or valine, or mixtures thereof, at 5-50 g/kg. As such their combination fails to render the invention as claimed obvious.

In view of the foregoing amendments and remarks, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a) over the combination of Richardson and Gordon.

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 101551.55779US).

Respectfully submitted,

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